REMARKS

I. Claims in the Case

Claims 19-30 are pending and under examination. Claims 19, 21, 22, 23, 25-30 have been amended and no claims have been added.

II. Specification

The title has been amended in a manner believed to the responsive to the Examiner's request. The specification has also been amended as suggested by the Examiner.

III. Priority

The Action sets forth its understanding of the priority entitlements. As it is not relevant to Applicants response, Applicants neither agree nor disagree with the Examiner's allegations regarding priority entitlement. Applicants will take a position if and when it becomes necessary.

IV. Claim Rejections -- §112, second paragraph

The Action first rejects various claims as indefinite under 35 U.S.C. §112, second paragraph. Applicants provide the following response.

Claim 27 has been amended as suggested.

Claims 21, 22, 25, 26, 29 and 30 have been amended in a manner that is believed to address the Action's concerns.

The Action's rejection of claims 19-30 is not entirely understood, as many of these claims clearly set forth the designation "I.U." for "international units." In any event, those claims that did not so set forth have been amended, which should obviate the rejection.

V. Claim Rejections -- §112, first paragraph

The Action nest rejects claims 19-22 and lacking enablement under 35 U.S.C. §112, first paragraph, with the Action alleging that there is no basis or experimental data to support the conclusion that oral IFNα can be used to "prevent destructive joint disease." Applicants traverse and provide the following response.

Example 36 demonstrates the results of an open label phase I study of orally ingested IFNα in the treatment of rheumatoid arthritis ("RA") patients. As can be seen, the compilation of results in Table 2 show that is 3 of the 4 patients treated there was substantial improvement (viz, halting of progression) in terms of both joint pain and joint swelling. As noted in paragraph [0190], the rationale for the foregoing studies was precisely to demonstrate usefulness in preventing the development of destructive joint disease:

> [0190] The rationale for treatment of RA by ingested IFN-α is that a proportion of RA patients will eventually develop destructive joint disease. The goal of therapy is to provide an agent that is readily accepted by patients, that is non-toxic so that it can be considered for use in the earliest stage of the disease process, is administered frequently without inconvenience, may prevent destructive phase of the disease, and neither induce nor be abrogated by the presence of circulating IFN neutralizing antibodies.

Specification, page 19 (of published application).

The Action presents no reasoning or evidence to the contrary and no reason to question the truthfulness of the foregoing statements. As noted in MPEP 2164.04:

> The examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. If an examiner can provide reasons sufficient to create a reasonable doubt as to the accuracy of a particular broad statement put forward by applicant as enabling support for a claim, a rejection under 35 U.S.C. 112, first paragraph can be made. A specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of §112 unless

> there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Assuming that sufficient reason for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis. *In re Marzocchi*, 169 USPQ 367 (CCPA 1971).

MPEP 2164.04.

For the foregoing reasons, the Examiner is requested to withdraw the rejection.

VI. Claim Rejections – 35 U.S.C. §103

Claims 19-26

Claims 19-26 are first rejected as obvious over the combination of Shozawa *et al.* ("Shozawa") in view of Cummings '795 and Cummings '382. Applicants traverse.

As conceded by the Examiner, Shozawa specifically teaches the administration of IFNα only by intramuscular administration, and says nothing about whether RA is amenable to therapy by oral IFNα, and certainly nothing about what oral dosage would be effective.

Cummings '795 is of no help in this regard, and is actually quite irrelevant. Cummings '795 appears to be limited to a method of regulating appetite and efficiency of food utilization in cattle using bovine interferon, and we can find no disclosure whatsoever in Cummings '795 in any way relevant to RA. If the Examiner is aware of any such teaching, we would appreciate it being pointed out on the record. To bring this distinction into even more focus, the rejected claims have now been amended and are now more clearly concerned only with human therapy.

The Cummings '382 patent is relevant, but only relevant to demonstrate non-obviousness. Cummings '382, taken together with Cummings '795, teach that the appropriate dosages of oral IFNα vary dramatically, depending on the disease being treated. For example, in the case of the '795 patent, which concerns appetite control in animals, as pointed out by the

Examiner it teaches to use from 500 to 5000 IU/Kg. However, the '382 patent, which concerns, among other things, the treatment of RA, it is taught to use 0.01 to about 5 IU of IFNα per lb., which corresponds to about 0.02 to about 11 I.U. IFNα per kg. This dosage is ***substantially*** lower that the dosage found by the present inventors to be efficacious in the treatment of RA. The differences may well be attributable to the fact that the '382 patent is teaching a different method of administration from that claimed here – the '382 patent teaches simply to contact the oral mucosa with the IFNα, and does not teach or suggest "immediately swallowing" as required by the present claims (which are worded as such to distinguish over gargling or swishing in the mouth). Since the '382 patent is emphatic in its recitation of dosages, and the Applicants cannot find any teaching therein that would lead one to modify such dosage range, it is submitted that no prima facie obviousness rejection has been made.

Claims 27-30

Lastly, the Action rejects claims 27-30 as obvious over the combination of references discussed above, further in view of Aman *et al.* ("Aman").

Applicants incorporate by reference the arguments set forth above, noting that Aman fails to provide any teaching to modify the '382 patent to employ the much higher IFNα doses of the present claims.

VII. Conclusion

It is submitted that the foregoing response is a complete response to the outstanding official action, and that the case is now in condition for allowance. The Examiner is invited to contact the undersigned attorney at (512) 536-3055 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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